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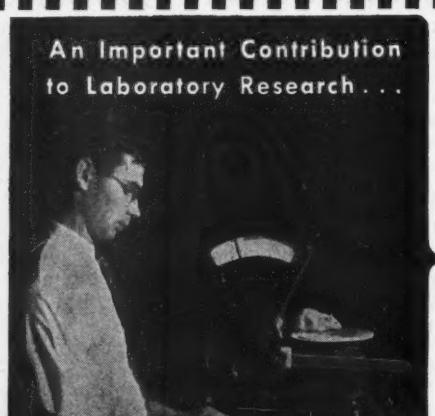

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ON THE Hr FACTOR AND THE Rh GENETIC THEORY

By Dr. PHILIP LEVINE

ORTHO RESEARCH FOUNDATION, LINDEN, N. J.

IN the recent discussions on the genetics of the Rh multiple alleles, no provision is, as yet, made for the role of a gene determining the Hr factor.[1,2] This agglutinable property was described very early in the course of the studies on the pathogenesis of erythroblastosis fetalis.[3] It was advisedly designated by Levine[4] as Hr (reversal of the letters Rh) because of peculiar relationship to a special variety of anti-Rh sera, now designated anti-Rh′. This is indicated in Table 1, which gives, at the same time, the four subtypes of Rh and their frequencies resulting from the reactions of anti-Rh_0 and anti-Rh′ sera.

From the beginning of the studies on erythroblastosis fetalis, Levine has held to the view that the relationship of the anti-Hr and anti-Rh′ sera is analogous to that of anti-M and anti-N sera. In other words, only three types of reactions are observed, and in both systems bloods failing to react with both anti-sera were never found. It was only after hundreds of bloods were tested that the term Hr and anti-Hr were designated. These results were not published more fully because it was clear that the first anti-Hr serum was of weak activity and gave too many negative reactions.

Subsequently, Race and Taylor described a similar

[1] R. R. Race, G. L. Taylor, K. E. Boorman and B. E. Dodd, *Nature*, 152: 563, 1943.

[2] A. S. Wiener, SCIENCE, 100: 595, 1944.

[3] P. Levine, L. Burnham, E. M. Katzin and P. Vogel, *Am. Jour. Obstet. and Gynec.*, 49: 925, 1941.

[4] P. Levine, Yearbook of Path. and Immunol., 508, 1941.

TABLE 1

BASED ON TESTS WITH 334 RANDOM BLOODS (WHITE) CARRIED OUT IN APRIL, MAY AND JUNE, 1941*

Terminology of Wiener and Landsteiner	Mrs. M.F. Anti-Rh_0	Mrs. M.S. Anti-Rh′	Mrs. K.F. Anti-Hr	Incidence of type (per cent.)
Rh_1	+	+	0 or ±	71
Rh_2	+	0	+	14
Rh′	0	+	0 or ±	2
Rh–	0	0	+	13

* At the written request of Dr. Wiener, the scheme of the reactions indicated was made available to him for inclusion in the third edition of his book, "Blood Groups and Transfusion," pp. 253–254 (C. C Thomas).

serum (called St) which contained more potent agglutinins.[5] These workers made the significant observations that individuals whose blood is Hr negative are homozygous for the Rh factor. At this point of their studies, only anti-Rh_0 sera were at their disposal so that they were not aware of the fact that all bloods of the subtype Rh_2, whether homozygous or heterozygous, react strongly with anti-Hr sera.[6] As pointed out by the writer,[7] individuals of the genotype Rh_1Rh_2, although heterozygous and reacting with anti-Hr sera, possess two dominant genes, Rh_1 and Rh_2, each determining the presence of a dominant agglutinable blood factor capable of inducing isoimmunization of the Rh negative mother. Accordingly, the genetically heterozygous Rh_1Rh_2 individual may be considered clinically as homozygous, since in matings with Rh negative women, all offspring must be Rh positive and therefore susceptible to erythroblastosis fetalis. These findings, published in 1943, are presented in Table 2, in which the gene determining the rare property Rh′ is not included.

TABLE 2

Phenotype	Genotype	Reaction with		
		Anti-Rh_0	Anti-Rh′	Anti-Hr
Rh_1	Rh_1Rh_1	+	+	0
	Rh_1Rh_2	+	+	±
	Rh_1rh	+	+	±
Rh_2	Rh_2Rh_2	+	0	+
	Rh_2rh	+	0	+
Rh–	rhrh	0	0	+

Nevertheless, the contribution of Race and Taylor is important because the genotype Rh_1Rh_1 is far more frequent than the genotype Rh_1Rh_2. With this observation, the analogy to the M and N relationship was still closer, since the homozygous M (MM) can not be differentiated from the heterozygous M (MN) with the aid of anti-M sera.[8] This differentiation can be made only with anti-N sera. Similarly, individuals of the genotype Rh_1Rh_1 can be recognized by the failure of their blood to react with potent anti-Hr sera.

The scheme given in Table 1 is now enlarged with the description of a third variety of anti-Rh serum reacting with 30 per cent. of random white individuals.[1,9,10] This serum subdivides, but in unequal portions, each of the four Rh varieties, thus making eight different subtypes of Rh.

Wiener[2] has stated that "the anti-Hr sera have a place in the scheme of Rh blood types similar to that of the anti-O sera in the blood group scheme." In support of his view, he states that ". . . anti-O sera, like anti-Hr sera, are usually of low potency." In this he obviously is in error, because anti-Hr sera are usually of weak activity because of statistical considerations and not out of genetic necessity. Levine[3,7] has shown that 92 per cent. of all mothers of erythroblastotic infants are Rh negative in tests with the potent diagnostic anti-Rh_0 sera. Of the remaining 8 per cent. Rh positive mothers, only a fraction (let us assume 3 per cent.[11]) are Hr negative and immunized by the Hr factor in fetal blood. It is, therefore, obvious that the chances for detecting equally potent anti-Hr and anti-Rh sera are 1:30. This value may be considered as tentative and the disproportion may be much greater because the Rh factor is far more antigenic than Hr. Actually, there are more incompatible matings for Hr (80 per cent. Hr+ × 20 per cent. Hr– or 16 per cent.) than for Rh (85 per cent. Rh+ × 15 per cent. Rh– or 13 per cent.).

In support of the views presented, Levine[12] has observed two potent anti-Hr sera, and reference to one of them has been reported elsewhere. Another anti-Hr serum now being investigated has a titer of at least 1:512, a value which approximates those of the most potent anti-Rh sera.[13]

This anti-Hr serum failed to yield quantitative titration differences of bloods homozygous and heterozygous for Hr factor. Qualitative differences, however, were observed, Rh negative and Rh_2 bloods giving stronger reactions. By analogy all bloods homozygous for N give stronger reactions with anti-N sera than the heterozygous type MN.

On purely theoretical grounds of a serologic nature, Wiener's views can not be accepted because anti-Hr and anti-Rh sera share the identical properties of origin (isoimmunization) and greater activity at 37° C. (warm agglutinins). Furthermore, there is no

[5] R. R. Race and G. L. Taylor, *Nature*, 152: 300, 1943.
[6] See Table 1.
[7] P. Levine, *Jour. Pediatrics*, 23: 656, 1943.
[8] K. Landsteiner and P. Levine, *Jour. Exp. Med.*, 48: 731, 1928.
[9] A. S. Wiener and E. B. Sonn, *Jour. Immunol.*, 47: 461, 1943.
[10] A. S. Wiener, SCIENCE, 54: 316, 1943.
[11] This value is probably too high.
[12] P. Levine, *Arch. Path.*, 32: 227, 1941.
[13] For this serum the writer is indebted to Dr. Peter Vogel.

reason to assume the existence of any differences in their pathological effects on the fetus and newborn infant. On the other hand, there are several striking characteristics which differentiate human anti-0 agglutinins from normal anti-A and anti-B isoagglutinins (incidence, potency and action at various temperatures). Certainly, there is no basis for excluding the Hr gene from any theory of the heredity of the various subtypes of the Rh factor.

Most workers believe that the Rh factor may be inherited as a series of multiple alleles, and indeed this is to be expected on the basis of past experience with agglutinable factors in animal blood detected by isoimmunization. It can be assumed that agglutinable properties detected by heteroimmunization like M and N exhibit simple genetic behavior in contrast to the agglutinable factors in chicken, rabbit and human blood detected by isoimmunization. In the latter group of the cases, the blood properties seem to be inherited as a series of multiple alleles.

Presumably, the Hr factor was not included in the Rh genetic scheme because it did not seem to fit into the theory originally suggested by Wiener on the basis of studies which, until very recently, did not include anti-Hr sera. Undoubtedly, the genetics of the Rh-Hr system may be still more complicated than is indicated in the schemes of Wiener, Race and Taylor.

Further support of this view was recently provided by Waller, Levine and Garrow,[14] who described an anti-Rh serum of unusual specificity, produced by an Rh_2 mother of an erythroblastotic infant. This serum contained an anti-Rh′ agglutinin, but in addition, an entirely new agglutinin which acted on some Rh_2 and many Rh negative bloods. Accordingly, this agglutinin was distinctly different in its specificity from anti-Rh″. Furthermore, the blood of this immunized woman reacted with anti-Rh″ sera.

In general, the experimental work in this field is hampered by the dearth of potent reagents of all varieties which must be derived mainly from immunized mothers, at best a most uncertain source. Workers are naturally tempted to carry out heredity and racial studies with whatever rare reagents may be available at the time. This is well illustrated in recent numerous publications on the Rh_2 factor carried out with a particular serum which contained anti-Rh″ but also anti-Rh_0 agglutinins. The dilution method for the separation of the anti-Rh″ agglutinin failed to give clear-cut differentiation.[15] Another example is the use of a weak anti-Hr agglutinin, the activity of which disappeared in the course of the study.[16]

[14] R. K. Waller, P. Levine and I. Garrow, *Am. Jour. Clin. Path.*, 14: 756, 1944.
[15] R. K. Waller and P. Levine, SCIENCE, 100: 453, 1944.
[16] A. S. Wiener, I. Davidsohn, and E. L. Potter, *Jour. Exp. Med.*, 81: 63, 1945.

Our knowledge of the Rh factor is slowly being extended so that no final theory can be accepted because the subject is still in a fluid state. The calculation of gene frequencies in support of the current theory of multiple alleles may perhaps be proven to be correct. On the other hand, such calculations may also be misleading as happened in the case of the two heredity theories of the four blood groups. Thus, the gene frequencies, on the basis of the now discarded theory of v. Dungern and Hirszfeld, seemed to fit the observed values obtained from studies of families and races. It is significant that the current theory of Bernstein was accepted as a result of statistical studies involving the rarest of the four blood groups, *i.e.*, AB. The state of affairs in the case of the genetics of the RhHr system is certainly far more involved, both from the point of view of technic and the availability of potent reagents. An additional complicating factor is the existence of several subtypes of remarkably low incidence.

Unfortunately, there are already several terminologies of the Rh subtypes, *i.e.*, those of Wiener[2] and Murray, Race and Taylor.[17] In the more or less distant future, it will undoubtedly become necessary for an international committee of geneticists and serologists to recommend a uniform terminology. This, however, can be done only after the analysis of family and racial studies, carried out with all varieties of maximally active reagents. Such studies must, of necessity, be on a vast scale in order to evaluate the role of the very rare subtypes, determined by the factors Rh′, Rh″ and the new factor of Waller, Levine and Garrow.

Because this subject is clinically important, one can hardly expect the clinician to commit to memory at this stage several genetic schemes of phenotypes and genotypes. Fortunately, this is not necessary, nor indeed, is it desirable. It follows from the statistical studies of mothers of erythroblastotic infants and the direct correlation of the frequency of erythroblastosis fetalis in any race to the incidence of Rh negative individuals,[18, 19] that the anti-Rh_0 serum is the most important single reagent for the diagnosis of erythroblastosis fetalis and prevention of the associated and frequently fatal intra-group transfusion reactions. Ninety-two per cent. of all mothers of erythroblastotic infants are Rh negative in tests with the diagnostic anti-Rh_0 serum. In order to produce evidence of isoimmunization in the remaining 8 per cent. of Rh positive mothers of erythroblastotic infants, at least three different blood factors may be involved, (1) the prop-

[17] J. Murray, R. R. Race and G. L. Taylor, *Nature*, 155: 112, 1945.
[18] P. Levine, SCIENCE, 96: 452, 1942.
[19] P. Levine and H. Wong, *Am. Jour. Obstet. and Gynec.*, 45: 832, 1943.

erties A or B of fetal blood, non-secretor type, (2) the Hr factor and (3) finer differences of the Rh factor. The report to the clinician in the exceptional Rh positive mothers can be worded as an incompatibility detected by a particular reagent. In any event, it will be necessary for these bloods to be referred to a serologic specialist who may or may not have on hand potent anti-Hr and the other two varieties of anti-Rh sera. So far as the clinician is concerned, one may recommend the simple genetic theory based on the behavior of the diagnostic (anti-Rh_0) serum, which contains but a single antibody. A more detailed analysis which requires the use of other anti-Rh sera or anti-Hr serum can be supplied by the specialist in the field.

SCIENTIFIC EVENTS

THE IPATIEFF HIGH PRESSURE AND CATALYTIC LABORATORY OF NORTHWESTERN UNIVERSITY

THE funds for the founding of the High Pressure and Catalytic Laboratory came from Northwestern University and private sources. A part of the apparatus was contributed by the Universal Oil Products Company. The idea for such a laboratory was sponsored by Professor W. V. Evans, of the department of chemistry, and permission to establish such a laboratory was obtained from the president of the university. The aims of the laboratory have been:

1. To study catalytic reactions under normal and high pressures because of their theoretical as well as their industrial importance.
2. To give students in chemistry and engineering not only theoretical but practical knowledge of the main types of catalytic reactions and the properties of catalysts.

During the first five years of the existence of the laboratory the work has dealt mainly with the application of catalysts in the field of terpenes, as follows:

1. A method for obtaining terpenes from solutions of terpene alcohols by dehydration in the presence of very dilute inorganic salts such as magnesium chloride, ammonia chloride, etc.
2. A new method of determining the presence of three, four and five methylene rings in di-cyclic terpenes.
3. A study of alkylation of terpenes with aromatics in the presence of various catalysts.
4. A new cyclic isomerization of limonene into a new di-cyclic terpene.
5. A study of the transfer of hydrogen in the terpene series in the presence of no hydrogenation catalyst.

From the student's point of view the following programs are in progress:

A. Students perform experiments on hydrogenation, oxidation, isomerization, polymerization, alkylation, etc.
B. They become acquainted with and prepare the main types of catalysts.

The equipment of the laboratory consists of the following:

1. Ipatieff type bombs of various sizes and models which can withstand pressures up to 400 atmospheres at 500° C. temperature.
2. Special type bombs for the study of the solubility of gases and critical temperatures, which allow the removal of small portions of the reactants during the reaction for study.
3. Turbo mixer type bombs which rapidly mix the reactants during a reaction.
4. Special apparatus for the study of continuous reactions under pressures up to 130 atmospheres.
5. Special bomb-proof units where these high pressure reactions can be carried out.

The laboratory is under the control of Dr. V. N. Ipatieff, an authority on high pressure reactions and a pioneer in the field of catalysis.

Dr. Ipatieff is assisted by Professor Pines, who gives lectures on catalysis in the department of chemistry. Professor Pines has been associated with Professor Ipatieff in his major discoveries of the past fifteen years.

The war has interfered with the development of this laboratory both by taking away prospective students and by making it impossible to secure needed apparatus. As soon as it is possible to do so, the laboratory will be enlarged, and its accommodations increased. A large number of students and research associates taking graduate work along the lines of catalysis and high pressure are expected to take part.

NEW LECTURE ROOM VISUAL AIDS AT COLORADO AGRICULTURAL AND MECHANICAL COLLEGE

EIGHTEEN mural paintings depicting the epochs of geologic time through representations of various plants and animals from the pre-Devonian period through succeeding epochs to modern times have been painted on 500 square feet of the walls of the botany building lecture room at the Agricultural and Mechanical College, Fort Collins, Colo.

Since they were painted during the summer of 1944, the murals have continued to attract increased attention and have been accorded growing favorable comment by students, faculty and visiting botanists and geologists.

The 7-foot panels done in oil by Dr. L. W. Durrell,

member of the college staff for the past twenty-one years and recently appointed dean of the division of science and arts after being head of the department of botany and plant pathology since 1924, picture the giant tree ferns, horsetails and other plants of the coal measures. These are followed by representations of cycads and pines. Of the extinct animals, dinosaurs, pterodactyls, three- and four-toed horses, four-tusked elephants and woolly mammoths, the saber-toothed tiger and the great bison are represented.

Dr. Durrell harmonized his murals with a predominance of greens and tans. His compliance with color perspective and with psychological perspective added depth to the scenes he portrayed.

Intended for a teaching device, Dr. Durrell credits his inspiration for the murals to those of Charles R. Knight, who has done large mural paintings of prehistoric men and animals for the American Museum of Natural History, New York City; the Los Angeles Museum, the Field Museum, Chicago, and the National Museum, Washington, D. C.—G. E. F.

THE NEW ENGLAND ASSOCIATION OF CHEMISTRY TEACHERS

THE seventh annual summer conference of the New England Association of Chemistry Teachers is planned for August 9 to 13 at the Massachusetts State College at Amherst.

The subject of the annual symposium will be "Chemical Equilibrium." It will be conducted by Professor A. R. Davis, of the Massachusetts Institute of Technology, and a group of secondary school teachers of chemistry.

Although the summer conference is held principally for the benefit of members of the association, any one interested will be welcome. Housing will be available at the college. Families of teachers will find Amherst an interesting spot, since it is in one of the most picturesque sections of the Connecticut Valley. The Massachusetts State College, founded by the Morrill Act of 1862, was opened to students in 1867. The campus consists of 700 acres, about a mile from the center of Amherst. There is also a demonstration forest of 750 acres six miles north on Mt. Tobey. Amherst is eighty-eight miles from Boston and may be reached by the Central Vermont Railroad or by bus connections from Northampton, Holyoke, Greenfield and Springfield.

Details concerning fees and the program will be included in the report of the association to be published in the July issue of *The Journal of Chemical Education*. All communications concerning the conference should be addressed to the secretary, Miss Dorothy W. Gifford, Lincoln School, Providence 6, R. I.

WARE CATTELL VS. THE AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE SETTLED FOR $7,500 BY CONSENT JUDGMENT

ON July 12, 1943, Ware Cattell was dismissed by the Executive Committee of the American Association for the Advancement of Science from his position as Editor of *The Scientific Monthly*. Mr. Cattell brought suit alleging breach of contract, asking damages for the remaining three and one-half years of that contract in the amount of $17,500.

The case came on to trial on January 8, 1945. Mr. Cattell testified on his own behalf and rested his case. The following officers testified on behalf of the Association: Dr. Isaiah Bowman, President in 1943; Dr. Otis W. Caldwell, General Secretary; Mr. Sam Woodley, Assistant Secretary. The Captain of the Guard of the Smithsonian Institution also testified.

On the fourth day of the trial, settlement negotiations were initiated. Following several conferences among the Court, the parties and their counsel, a settlement was agreed upon whereby the Court awarded a consent judgment to Mr. Cattell in the amount of $7,500.

It was part of the agreement between the Association and Mr. Cattell that Mr. Cattell waived all further legal claims with reference to his dismissal as Editor of *The Scientific Monthly*.

The following Stipulation of Settlement was entered in the cause:

It is hereby stipulated by and between the parties to this action, by their attorneys, that this action be finally settled upon the following basis:

1. That in full payment, settlement and discharge of all claims and damages, actions and causes of action for, upon, or by reason of any damages, costs, expenses and compensation which have been or which hereafter may be sustained by the plaintiff, Ware Cattell, on account of or in any way growing out of it, resulting from or to result from any acts or actions of the defendant corporation, American Association for the Advancement of Science, or any of its officers, agents, servants or employees, to the date of the execution of this Stipulation of Settlement, intending to include herein among all other claims and demands, actions and causes of action, all claims and demands, actions and causes of action for, upon or by reason of the act and actions of the defendant corporation, American Association for the Advancement of Science, and any of its officers, agents, servants and employees, in the matter of the termination as of July 12, 1943, of the appointment of the plaintiff, Ware Cattell, as Editor of *The Scientific Monthy*, and in all other employment capacities whatsoever, and in full settlement, payment and discharge of this action, Civil Action No. 21,508, the defendant, American Association for the Advancement of Science, agrees to pay the plain-

tiff, Ware Cattell, the sum of Seven Thousand Five Hundred Dollars ($7,500.00).

2. That the parties hereto consent that the Court enter judgment in the above-entitled action, in the sum of Seven Thousand Five Hundred Dollars ($7,500.00), in favor of the plaintiff, Ware Cattell, against the Association, for the aforesaid sum of Seven Thousand Five Hundred Dollars ($7,500.00), without interest and without costs.

(s) DAVID A. FEGAN, Attorney for the plaintiff, Ware Cattell.

(s) WARREN E. MAGEE, Attorney for the defendant, American Association for the Advancement of Science.

The foregoing Stipulation of Settlement in the above-entitled action, Civil Action No. 21,508, is hereby approved, and the Clerk of this Court shall, and he is hereby directed, to enter judgment pursuant to the terms of this Stipulation of Settlement, in favor of the plaintiff, Ware Cattell, and against the defendant, American Association for the Advancement of Science, for the aforesaid sum of Seven Thousand Five Hundred Dollars ($7,500.00), without interest and without costs.

(s) T. ALAN GOLDSBOROUGH
JUSTICE

Dated this 15th day of January, 1945.

SCIENTIFIC NOTES AND NEWS

THE degree of doctor of laws was conferred at the commencement exercises of the School of Medicine of Temple University, Philadelphia, on Dr. Charles F. Kettering, of the research laboratories of the General Motors Corporation, president of the American Association for the Advancement of Science.

THE honorary doctorate of science was conferred on June 23 at the commencement exercises of Princeton University on Sir Alexander Fleming, of the University of London, the discoverer of penicillin. A dinner, arrangements for which were made by Charles Pfizer & Co., Merck & Co. and E. R. Squibb & Sons, three of the original manufacturers of the drug, was given in his honor on June 25 at the Waldorf-Astoria, at which he made the principal address. The speakers included Dr. Vannevar Bush, director of the Office of Scientific Research and Development, and Dr. Alfred N. Richards, professor of pharmacology at the University of Pennsylvania, chairman of its medical research committee.

THE doctorate of science of Wesleyan University was conferred on June 24 on Dr. Leonard A. Maynard, director of the School of Nutrition and of the U. S. Nutrition Laboratory at the New York State College of Agriculture at Cornell University.

BATES COLLEGE conferred the degree of doctor of science at its seventy-ninth commencement on Thomas Spooner, director of research of the Westinghouse Electric and Manufacturing Company at East Pittsburgh.

THE honorary degree of doctor of laws was conferred on the occasion of the centennial commencement exercises of Baylor University on Brigadier General W. Lee Hart, U. S. Army, medical director of the Eighth Service Command.

THE doctorate of science was conferred on Dr. John L. Atlee, Jr., surgeon-in-chief of St. Joseph's Hospital, Lancaster, Pa., at the commencement exercises on June 24 of Franklin and Marshall College.

THE following have been cited by the University of Chicago as Distinguished Alumni: Dr. Charles H. Behre, Jr., professor of geology, Columbia University; Dr. Eloise B. Cram, senior zoologist, U. S. Public Health Service, Wash.; Dr. Melville J. Herskovitz, professor of anthropology, Northwestern University, and Walther Loehwing, professor of botany, the State University of Iowa.

THE James Alfred Ewing Medal for 1944 has been awarded to B. N. Wallis, F.R.S., chief of aeronautical research and development of Vickers-Armstrongs, Limited, by the Council of the British Institution of Civil Engineers, on the joint recommendation of the presidents of the Royal Society and the Institution of Civil Engineers. He invented and designed the special type bombs used for the destruction of the Moehne and Eder dams in Germany in 1943, and designed the Tallboy and ten-ton bombs used by the R.A.F. He was responsible for the design and construction of the rigid airship R 100.

THE Chapter of the Society of Sigma Xi at the University of Southern California has elected the following officers for 1945–46: Howard de Forest, *President;* John Dodge, *Vice-president;* Robert I. Rutherford, *Treasurer,* and Winslow Whitney Smith, *Secretary.*

THE Hawaiian Academy of Science held the final sessions of its twentieth annual meeting on May 3, 4 and 5, at the University of Hawaii, Honolulu. The first two evenings were devoted to papers in the fields of chemistry, animal parasitology, ecology of fish, growth of pineapples and organization of agricultural research. Also included were two papers in social science dealing with war-time public opinion and morale. The last evening was given over to a busi-

ness meeting; to the address of the retiring president, J. L. Collins, on "Inter-Specific Hybrids in Ananas comosus (Pineapple)," and to a social gathering of members and their friends. Officers elected were: *President,* Peter H. Buck; *Vice-president,* Thomas A. Jaggar, Jr.; *Secretary-Treasurer,* Chester K. Wentworth; *Councilors,* Colin G. Lennox, one year; Christopher J. Hamre, two years; J. L. Collins, *ex officio.*

THE thirtieth annual meeting of the South Dakota Academy of Science was held on May 4 and 5 at Mitchell, S. D. Officers elected for the year 1945–46 are as follows: *President,* Raymond J. Greb, Huron College; *First Vice-president,* F. L. Bennett, Black Hills Teachers College; *Second Vice-president,* Ernest Griswold, University of South Dakota; *Secretary-Treasurer,* A. L. Haines, Vermillion, S. D. The address, given by Dr. C. H. Werkman, of the department of bacteriology of Iowa State College, was entitled "Metabolic Marvels of the Living Cell." The next annual meeting will be held at Augustana College, Sioux Falls, S. D.

THE annual initiation and dinner of the Mayo Foundation Chapter of the Sigma Xi held on June 7 marked the twenty-fifth anniversary of the founding of the chapter. The meeting was attended by ninety-four members. Dr. A. H. Sanford, first president of the chapter, addressed the initiates and members and outlined its founding and early history. Dr. H. E. Essex, president for the 1944–45 season, gave the annual presidential address. His topic was "Serigraphy." Officers elected for the 1945–46 season are: *President,* Dr. A. R. Barnes; *Vice-president,* Dr. H. W. Woltman, and *Secretary-Treasurer,* Dr. C. F. Code.

SIR FRANK SMITH has been elected president of the British Institute of Physics; Professor A. M. Tyndall, vice-president; Major C. E. S. Phillips, honorary treasurer, and Professor J. A. Crowther, honorary secretary.

PROFESSOR DOUGLAS HAY, managing director of the Barrow Barnsley Main Collieries, Ltd., honorary professor of mining, and a member of the council of the University of Sheffield, has been elected president of the British Institution of Mining Engineers.

SIR JOHN ORR, professor of agriculture in the University of Aberdeen, has been elected a member of Parliament for the Scottish universities.

AMONG members of the faculty of the University of Wisconsin who retire at the end of the present academic year are Dr. C. K. Leith, professor of geology; Dr. W. H. Twenhofel, professor of geology and chairman of the department; Dr. M. F. Guyer, professor of zoology; Dr. Edwin B. Hart, professor of biochemistry, and Harry D. Tiemann, associated with the Forest Products Laboratory and lecturer in forest products at the university.

IT is reported in *The Lancet* that Professor M. Greenwood, F.R.S., will retire from the chair of epidemiology and vital statistics at the School of Hygiene of the University of London. Owing to a change in the distribution of teaching and the steady increase in the volume of research work and teaching within the field of medical statistics, the title of the chair has been altered to that of medical statistics, and Dr. A. Bradford Hill, since 1933 reader in medical statistics in the university, has been appointed to fill the vacancy. The senate has conferred the title of professor emeritus in epidemiology and vital statistics on Dr. Greenwood.

DR. WALLER S. LEATHERS, professor of preventive medicine and public health and since 1928 dean of the School of Medicine of Vanderbilt University, will retire on June 30. He will be succeeded by Dr. Ernest W. Goodpasture, associate dean and since 1924 professor of pathology at the school. Dr. Sam L. Clark, professor of anatomy, has been appointed associate dean. Dr. William W. Frye, associate professor, has been promoted to a professorship and becomes head of the department of preventive medicine and public health.

DR. HANFORD TIFFANY, chairman of the department of botany of Northwestern University, has been appointed William Deering professor of botany, and Dr. N. E. Bingham, of Temple University, and Dr. O. J. Eigsti, of the University of Oklahoma, have been appointed associate professors. Dr. M. S. Doty, of Stanford University, has been appointed instructor, and Dr. Francis Drouet, of the Chicago Natural History Museum (formerly Field Museum), research associate.

DR. HARDY L. SHIRLEY, director of the Northeastern Forest Experiment Station of the U. S. Forest Service at Philadelphia, has been made assistant dean of the New York State College of Forestry at Syracuse University. Dr. Shirley will take up the work on September 1. He succeeds Clyde Leavitt, who retired in November, 1943.

AN Associated Press dispatch states that M. Georges Claude, the French chemist and physicist, since 1924 a member of the Paris Academy of Sciences, has been sentenced to life imprisonment as a Nazi collaborationist.

DR. ANDREY AVINOFF, since 1926 director of the Carnegie Museum at Pittsburgh, has resigned for reasons of health. The title emeritus has been conferred on him.

DR. W. V. LAMBERT, who recently was appointed assistant research administrator in the Agricultural Research Administration of the U. S. Department of Agriculture, has resigned as secretary-treasurer of the American Society of Animal Production, of which Dr. A. D. Weber, head of the department of animal husbandry of Kansas State College, Manhattan, is president. The executive committee has appointed Dr. W. G. Kammlade, of the department of animal husbandry of the University of Illinois, secretary-treasurer, the appointment to be effective at once. Dr. Kammlade also will serve as business manager of the *Journal of Animal Science*, which is published quarterly by the American Society of Animal Production.

FRANK E. MURPHY, assistant to the manager of research of the development division of the Research and Development Department of the Pennsylvania Salt Manufacturing Company, Philadelphia, has been made director. He will have charge of chemical engineering activities, including pilot plant operations, engineering research and related fields of work. His headquarters will be at the Whitemarsh Research Laboratories.

DR. PIERRE DANSEREAU, director of the Service de Biogéographie at the Université de Montréal, will leave for Brazil in July for a one-year research fellowship awarded by the Brazilian government.

DR. A. C. GOODINGS, of the Ontario Research Foundation; B. H. Wilson, director of the British Wool Industries Research Association; Professor J. B. Speakman, of the University of Leeds; and Dr. F. T. Peirce, of the British Cotton Industries Research Association, are visiting Australia by invitation of the Commonwealth Government to assist in formulating plans for research designed to help Australian and overseas manufacturers and processors of wool.

DR. HERBERT C. HANSON, formerly general manager of the Alaska Rural Rehabilitation Corporation, is leaving shortly for Norway as Agricultural Rehabilitation Officer for the UNRRA.

DR. OLOF LARSELL, professor of anatomy at the School of Medicine at Portland of the University of Oregon, gave on May 11 at the School of Medicine of the University of Minnesota the first J. B. Johnston Lecture on neurology. His subject was "Comparative Neurology and Our Present Knowledge of the Cerebellum."

THE De Lamar Lecture in Hygiene at the Johns Hopkins University School of Hygiene and Public Health was given on May 17 by Dr. George Baehr, clinical professor of medicine at the College of Physicians and Surgeons, New York. He spoke on "Medical Service under the Health Insurance Plan of Greater New York."

VICE ADMIRAL ROSS T. MCINTIRE, Surgeon General of the U. S. Navy, and Dr. James L. Morrill, president-elect of the University of Minnesota, were the speakers at a dinner meeting held on June 5 under the sponsorship of the committee of founders of the Mayo Memorial. The subject of the meeting was "Health and Medicine in War and Peace."

THE National Research Council is anxious to obtain data on the composition of foreign foods, particularly Far Eastern Foods, and earnestly solicits such information. Address communications to Dr. L. J. Teply, secretary of the Committee on Food Composition and of the Committee on International Food Value Problems, Food and Nutrition Board, National Research Council, 2101 Constitution Avenue, Washington 25, D. C.

THE Ohio State University has received gifts and bequests amounting to $20,175. The largest of these gifts was the sum of $6,500 for the College of Medicine.

DR. H. A. B. DUNNING, of Hynson, Wescott and Dunning, Inc., of Baltimore, Md., has given to the department of pharmacology of the Medical School of the University of Maryland the sum of one thousand dollars to be used for research.

A SEED storage and processing plant for the handling of inbred lines and single crosses is being constructed at the University Farm of the Department of Agriculture of the University of Minnesota. The building will be used almost entirely for the handling of inbred lines of corn and single crosses that are used in the hybrid varieties recommended by the Minnesota Experiment Station. In Minnesota the inbred lines used in varieties bred by the station remain under its control, and single crosses used by seed growers in producing double crossed seed of station recommended hybrids are produced under its immediate supervision.

A SURVEY in the field of biogeochemistry will be sponsored by the American Museum of Natural History. A preliminary three-year study has been made possible by gifts received from Robert Earl McConnell, trustee of the museum, and George M. Moffett, president of the Corn Products Refining Company. Dr. G. Evelyn Hutchinson, professor of zoology at Yale University and consultant in biogeochemistry of the museum, will direct the survey with the cooperation of various specialists.

IT is reported in the *Experiment Station Record* that the University of Minnesota has entered into an

agreement with the newly organized Mayo Forestry and Horticultural Institute whereby several tracts of land will be made available to the university for research and demonstration in forestry and horticulture. The Mayo Properties Association has appropriated $25,000 for tools, labor and planting materials. The forestry work will occupy about 140 acres of land in or near Rochester, Minn., mostly on property of the Institute of Experimental Medicine, and will include studies on erosion control in cooperation with the Soil Conservation Service of the U. S. Department of Agriculture. The university division of horticulture plans to use about 40 acres of this tract, originally developed as an orchard under private ownership prior to its donation in 1943 to the Mayo Properties Association. Variety tests and demonstrations with apples are to be continued and enlarged, and several acres will be used for small fruit plantings. W. H. Alderman, chief of the division of horticulture, has been given charge of the fruits projects, and Dean Henry Schmitz, of the College of Agriculture, Forestry and Home Economics, of the forestry areas.

SPECIAL ARTICLES

LYCOPERSICIN, A FUNGISTATIC AGENT FROM THE TOMATO PLANT

FUSARIUM wilt, caused by *Fusarium oxysporum* f. *lycopersici* (Snyder and Hansen),[1] is one of the most prevalent and damaging diseases of tomatoes in many regions of the United States. The mechanism of the wilting caused by this vascular parasite is obscure, but wilting of tomato plants infected with *F. oxysporum* f. *lycopersici* (hereafter designated Fol.) can be correlated with the presence in the tracheal fluid of the host of a toxin which is presumably elaborated by the fungus.[2] Since tomato varieties vary in their susceptibility to Fusarium wilt[3] it might be postulated variously that (1) certain varieties are wilt-resistant because they are able to produce a substance or substances which either neutralize the toxin directly or inhibit the growth of the fungus; (2) certain varieties are susceptible because they produce a substance or substances that promote or make possible growth of the parasite, or (3) differences in susceptibility or resistance are due to differences in amounts of such substances common to both categories of plants. Fisher[4] and more recently Gottlieb[5] have obtained evidence to indicate that the expressed juice from tomato plants retards growth of Fol. in culture in proportion to the wilt-resistance of the tomato varieties tested.

In this laboratory we have obtained from the expressed juice of Pan America tomato plants, a variety which exhibits a high degree of wilt resistance,[6] a preparation which, though still impure, possesses marked fungistatic activity toward Fol. This antibiotic agent, which will be designated "lycopersicin," occurs throughout the mature plant. In the crude preparations available, lycopersicin is completely stable, as indicated by assay, for at least 1 hour at 100° C and withstands autoclaving for at least 15 minutes at 15 pounds pressure. It is dialyzable (Visking, Cellophane membrane), adsorbed from aqueous solution at pH 5.5 on charcoal (unactivated Norit A), soluble in water and methanol, partially soluble in ethanol, and insoluble in chloroform, acetone, ethyl acetate, ether, petroleum ether and benzene.

A rapid and accurate method for the assay of the fungistatic activity of lycopersicin, patterned after the cylinder-plate method now used for the assay of penicillin and related antibiotic agents,[7] has been developed. Sterile, 90 mm Petri dishes, containing 20 ml of solidified Czapek-dextrose agar,[8] are warmed to approximately 45° C. and flooded with 3.5 ml of a suspension of spores of Fol.[9] in the same medium. To prepare the inoculum 5 ml of sterile distilled water are added to a 5-day-old potato-dextrose slant of the organism and the surface is gently stroked with a sterile loop to yield a heavy aqueous suspension of spores. The suspension is filtered through a thin, sterile cotton plug (to remove bits of mycelium which, if allowed to remain, give rise to growth irregularities on the assay plate) into 40 ml of Czapek-dextrose agar maintained at 45° C. After thorough mixing, the inoculum is flooded evenly over the agar surface in the Petri dish and is allowed to solidify. Porcelain

[1] Synonymous with *Fusarium bulbigenum* var. *lycopersici* (Brushi) Wr. and R.

[2] D. Gottlieb, *Phytopathology*, 34: 41, 1944.

[3] W. S. Porte and F. L. Wellman, *U. S. Dept. Agr. Circ.* No. 584: 1941.

[4] P. L. Fisher, *Maryland Agr. Expt. Sta. Bul.* 374: 1935.

[5] D. Gottlieb, *Phytopathology*, 33: 1111, 1943.

[6] W. S. Porte and H. B. Walker, *U. S. Dept. Agr. Circ.* No. 611: 1941.

[7] W. H. Schmidt and A. J. Moyer, *Jour. Bact.*, 47: 1, 1944.

[8] $NaNO_3$, 3.0 g; $K_2HPO_4 \cdot 3H_2O$, 1.0 g; $MgSO_4 \cdot 7H_2O$, 0.5 g; KCl, 0.5 g; $FeSO_4 \cdot 7H_2O$, 0.01 g; dextrose, 30 g; agar, 20 g; water, 1,000 ml.

[9] The culture used throughout this work was a transfer from the R-5-6 strain of Wellman (*Phytopathology* 32: 271, 1942) that was originally selected for its high pathogenicity. At the start of the present investigation a large stock of lyophil tubes of spores of this organism was prepared (see method of Raper and Alexander to be published in *Mycologia*, July-August, 1945) from vigorously growing potato-dextrose agar slants. To obtain the spores necessary for preparing inoculum for the assay plates potato-dextrose slants are inoculated weekly from a newly broken lyophil tube. In this manner the source of inoculum for the assay plates is maintained constant both as to age and virulence and the danger of introducing contaminants is minimized.

cylinders of the type used for penicillin assay (8 mm outside diameter, 10 mm high)[10] are dropped on the inoculated surface and the covered plate is incubated for 24 hours at 28° C. in a constant temperature incubator equipped for continuous air circulation. The solutions to be assayed are pipetted into the cylinders and the plates are incubated for an additional 16 hours under the same conditions, after which the inhibition zones are measured.

Growth of the fungus on plates prepared in this manner is uniformly raised, white and cottony, and develops evenly and spontaneously over the entire agar surface. Inhibition zones surrounding the cylinders are sharply defined and can be measured accurately. Control cylinders, filled with water, show no evidence of inhibition. Plates to which the test solution is added before 20 hours or after 30 hours of incubation show less distinct inhibition zones than those to which test solutions are added after the optimum period of incubation, namely, 23 to 25 hours after inoculation. Inhibition zones must be measured within 15 to 17 hours after the test solutions have been applied. After periods of less than 15 hours the inhibition zones are not well defined due to the thinness of the fungus mat; after more than 17 hours, overgrowth of the edges of the inhibited zones may occur.

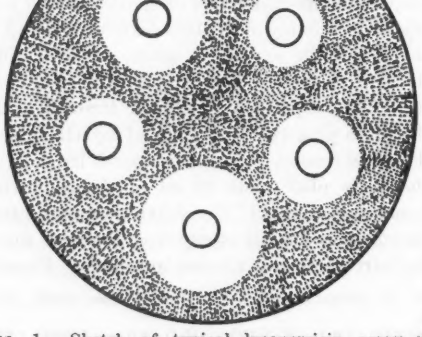

FIG. 1. Sketch of typical lycopersicin assay plate showing inhibition zones produced by several dilutions of the standard solution. Reading clockwise from the bottom the cylinders contain 10, 1, 5, 0.5 and 2 lycopersicin units per ml, respectively.

A typical assay plate illustrating the gradation in response produced by dilutions of an arbitrarily established standard solution[11] is shown in Fig. 1. The standard solution and 19 dilutions of the standard solution were assayed repeatedly and the average diameters of the inhibition zones produced by each concentration of the standard were used in constructing the standard curve shown in Fig. 2. The diameter

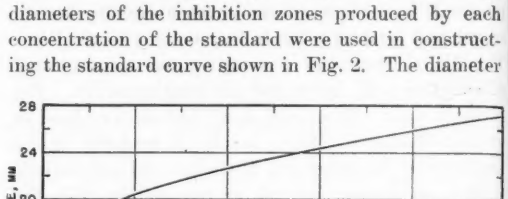

FIG. 2. Standard curve for lycopersicin assay. Lower curve represents an expanded plot of the left hand portion of the upper curve.

of the inhibition zone produced by a given solution was found to be reproducible within narrow limits. For example, the diameters obtained in replicate tests on different plates for one of the solutions used were 23.2, 23.9, 23.7, 24.0, average 23.7 mm. In constructing the curve shown in Fig. 2 one of the dilutions of the standard solution was arbitrarily considered to contain one lycopersicin unit per ml and points for other dilutions of the standard solution were plotted accordingly. Under the conditions described a solution containing one unit of lycopersicin per ml will produce an inhibition zone of approximately 18.5 mm. Comparable assays can be obtained using this arbitrary standard until the isolation of lycopersicin makes it possible to evaluate the unit in terms of the weight of pure compound required to effect equivalent inhibition.

It will be realized that at least a part of the standard curve represented in Fig. 2 must be redetermined for each series of assays to compensate for variations in the standard response. The curve in Fig. 2 is only representative of a family of curves having the same shape but in which the individual curves may lie slightly above or below the one shown. Accuracy of assays by this technique appear to be of the same order of magnitude found for the assay of penicillin[7] and the method is subject to similar limitations.

By use of the standard and standard curve described it has been possible to assay the various parts

[10] Fisher Scientific Company, "Penicylinders."

[11] The standard solution was prepared as follows. Thoroughly washed, mature Pan American tomato plants (115 days old), including the roots but not the fruit, were dried, finely ground and extracted by refluxing with methanol. The methanol extract was concentrated to dryness, the residue was extracted with water and the aqueous extract was lyophilized to dryness. A dilute aqueous solution of the dry material was distributed in 1.5 ml portions among several Pyrex ampoules and the sealed ampoules were autoclaved for 15 minutes at 15 pounds pressure. This standard solution appears to be stable indefinitely when stored in the refrigerator.

of different tomato varieties for lycopersicin activity at all stages of growth from the seed to maturity. For this purpose the mechanically expressed, sterilized juice or sterile aqueous extracts of the plant tissue are placed directly in the assay cylinder. Sufficient data have not been obtained as yet to justify definite conclusions regarding the relative amounts of lycopersicin present in the materials which have been assayed; but it may be concluded that: (a) of the tomato varieties tested, including Bonny Best (highly susceptible to Fusarium wilt), Rutgers and Marglobe (resistant), Pan America and Red Currant (highly resistant), all contain the inhibitor; (b) lycopersicin activity, while absent in the seed, appears in seedlings germinated in the dark and in the plant within 8 days after planting; (c) the concentration of lycopersicin varies somewhat with the age of the plant and considerably with the plant part assayed. Results of these investigations, as well as consideration of the relationship between lycopersicin and the Fusarium wilt of tomatoes and consideration of the specificity of lycopersicin will be reported elsewhere.

The authors wish to express their appreciation to Dr. O. E. May, chief of the Bureau of Agricultural and Industrial Chemistry, for suggesting these investigations. Thanks are due Dr. K. B. Raper, Mr. W. H. Schmidt and Miss Dorothy F. Alexander for their cooperation and advice; and to Mr. O. W. Eady for technical assistance.

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ASPERGILLUS USTUS

THERE are now in the literature several reports of antibiotics active *in vitro* against *Mycobacterium tuberculosis*. They have been derived from culture filtrates of a variety of molds including *Aspergillus fumigatus*,[1,2,3] *Actinomyces griseus*[4,5] and one of the Penicillium group.[6] The present report will describe yet another.

Early in 1944, while systematically examining the antibiotic-producing properties of a number of fungi appearing as contaminants on routine culture plates, we came upon one which made its culture medium highly active against *M. tuberculosis*. It has subsequently been identified[7] as a strain of *Aspergillus ustus*, (Bain) Thom and Church, and examined more completely for its several properties.

The mold grows well on Czapek-Dox medium with 4 per cent. glucose and 0.1 per cent. Bacto-Yeast extract added. After 36 hours' culture there appears on the surface of the medium a thin veil-like growth which on the following day or two assumes a pale blue-green color. As the spores begin to develop the growth becomes more intensely green, and ultimately forms a brown wrinkled membrane. Frequently one may observe numerous clear yellow droplets on the surface of the culture. The temperature for the optimal production of the antibiotic substance appears to be 28° C., but the fungus will grow over a wide range, including 37° C. With the progressive growth of the culture there is a gradual increase in pH of the medium from an initial 5.8 to a final value between 8.0 and 8.4.

The substance that inhibits the growth of *M. tuberculosis* can first be demonstrated on the sixth day of culture and continues to increase to a maximum concentration at 14 to 16 days. It can be extracted from the medium by the use of various solvents, such as ether, chloroform, acetone, or by adsorption onto Norit, followed by elution with ether. Extraction with ether at pH 8.0 to 8.4 yields a light yellow amorphous residue which is insoluble in water but soluble in either 1 per cent. sodium carbonate solution or 95 per cent. alcohol. The potency of this ether-extracted residue on the tubercle bacillus was determined by preparing serial dilutions of the dry crude residue in Long's synthetic medium and then planting on this medium a thin surface growth, approximately 7 mm in diameter, of *M. tuberculosis*, Strain H37. When examined after an incubation period of thirty days at 37° C., the tests usually showed complete inhibition of growth in dilutions varying from 1:200,000 to 1:400,000, but the activity of this ether extracted residue varied with each batch of substance tested. The controls, prepared in the same manner but without the addition of the residue, showed a heavy growth covering the entire surface of the medium at the end of thirty days. It is interesting to note that similar experiments conducted with *Mycobacterium ranae* showed that the growth of this organism was inhibited to the same extent as that of

[12] Division of Biologically Active Compounds, Bureau of Agricultural and Industrial Chemistry.

[13] Division of Fruit and Vegetable Crops and Diseases, Bureau of Plant Industry, Soils, and Agricultural Engineering.

[1] A. Vaudremer, *C. R. Soc. Biol.*, 73: 51, 1912; 74: 278 and 752, 1913.

[2] M. A. Soltys, *Nature*, 154: 550, 1944.

[3] Igor N. Asheshov and Frieda Strelitz, SCIENCE, 101: 120, 1945.

[4] S. A. Waksman, *Proc. S.N. Mayo Clinic*, 19: 537, 1944.

[5] S. A. Waksman and A. Scholz, *Ibid.*, 57: 244, 1944.

[6] D. K. Miller and A. C. Rekate, SCIENCE, 100: 172, 1944.

[7] A culture of the fungus was sent to Dr. Charles Thom, and we are grateful to him for the above classification.

the tubercle bacillus. Against *Staphylococcus* and *Streptococcus* it has only slight activity, and against *Escherichia coli* none at all.

The active agent, whatever its nature, is very stable, for it is not completely destroyed even when autoclaved at a pressure of fifteen pounds for fifteen minutes. The filtrates from cultures kept at 28° C. for three months still show activity, and samples of the residue from ether extraction kept at 8° C. for the same length of time lose none of their potency.

Preliminary tests on mice have indicated that the crude extract is relatively non-toxic. Between 6 and 8 mgms can be tolerated by a mouse.

The experiments thus far have shown that there is an additional fungus of the Aspergillus group from the culture filtrate of which a substance can be obtained that definitely inhibits the growth of *M. tuberculosis in vitro*. It seems desirable, before attempting to establish the value of the antibiotic substance in experimental tuberculosis to obtain it in a more pure form. Studies are in progress to this end.

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THE EFFECT OF CYSTEINE ON STREPTOMYCIN AND STREPTOTHRICIN

THE recent communication of Cavallito and Bailey[1] describing the complete or partial inactivation of a large number of antibiotics by cysteine prompted us to test the action of the latter on streptothricin and streptomycin concentrates.[2] It was found that streptomycin is inactivated by cysteine, whereas streptothricin is not. Streptomycin is also inactivated by 2-aminoethanethiol but not to any significant extent by thioglycollic acid. The inactivation experiments were carried out by adding neutral solutions of the organic sulfur compounds to known amounts of streptomycin or streptothricin dissolved in neutral phosphate buffer. After storing for several hours, the solutions were tested for antibiotic activity against *Bacillus subtilis* by the Oxford cup method.[3]

TABLE 1

EFFECT OF ORGANIC SULFUR COMPOUNDS ON ACTIVITY OF STREPTOMYCIN AND STREPTOTHRICIN SOLUTIONS

Concentration of organic sulfur compound (mg/ml)	Streptomycin assay (units/ml)	Streptothricin assay (units/ml)
Control (phosphate buffer)	49	52
Cysteine HCl		
0.13	39	..
0.25	29	..
0.50	4	42
1.00	0	..
2.50	..	52
5.00	..	54
2-Aminoethanethiol HCl		
0.50	12	40
2.50	4	57
5.00	0	59
Thioglycollic Acid		
0.50	31	41
2.50	39	40
3.00	26	30

[1] Cavallito and Bailey, SCIENCE, 100: 390, 1944.

[2] The activity of streptomycin concentrates varied from 80 units/mg to 600 units/mg; the activity of the streptothricin was 440 units/mg.

The difference in behavior of streptomycin and streptothricin toward cysteine is of interest and of particular significance in view of the microbiological similarity of the two substances.[4] With the use of cysteine one can not only differentiate the two antibiotics but estimate the relative amounts of each in mixtures of the two (Table 2).

TABLE 2

EFFECT OF CYSTEINE ON MIXTURES OF STREPTOMYCIN AND STREPTOTHRICIN

	Streptomycin added (units/ml)	Streptothricin added (units/ml)	Cysteine hydrochloride added (mg/ml)	Assayed activity (units/ml)
Solution I . . .	25	25	0	45
Solution II . .	100	0	2	0
Solution III .	100	8	2	9
Solution IV .	100	15	2	17
Solution V . .	50	50	1.3	45

The cysteine inactivation of streptomycin can be reversed by iodine; presumably cystine is formed during this process. To our knowledge, this is the first recorded instance of reversible cysteine inactivation of an antibiotic. The regeneration of the antibiotic activity of streptomycin solutions containing cysteine was carried out by shaking such solutions with small amounts of a carbon tetrachloride solution of iodine until no further decolorization occurred. The solutions were aerated to remove the organic solvent before assay. The recovery of activity was quantitative.

The observations thus far made indicate that the inactivation of streptomycin is reversible, not a property of the sulfhydryl group alone, nor is it limited to cysteine. A mechanism postulating either a reversible chemical reaction between the two substances or a competitive effect on metabolic processes would be consistent with these observations.

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THE MECHANISM OF PAIN IN TRIGEMINAL NEURALGIA[1]

TRIGEMINAL neuralgia (tic douloureux), an episodic, recurrent, unilateral pain syndrome, occurs for the

[3] Foster and Woodruff, *J. Bact.*, 45: 408–9 (1943).

[4] Waksman, Bugie and Schatz, *Proc. Staff Meetings Mayo Clinic*, 19: 537–548, 1944.

most part in persons over fifty years of age who may have vascular disorders such as arteriosclerosis, arterial hypertension, migraine or Meniere's syndrome. Series of attacks may occur during periods of anxiety, fatigue, tension or stress.

Various conceptions of this disorder have been presented.[2,3] Recent observations indicate a relation between tic douloureux and defects in cranial circulation. Thus, surgical procedures designed to induce cranial vasodilatation have in two instances eliminated tic douloureux for an indefinite period.[4,5] The administration of vasodilator agents has reduced both the frequency and intensity of attacks of tic.[6] Beta methylcholine chloride was effective in one patient.[6] Also, attacks of tic pain have been temporarily abolished by the inhalation of amyl nitrite, and the continued administration of nicotinic acid by mouth had longer lasting effect in seven patients.[7] On the other hand, attacks of pain have been precipitated in patients with trigeminal neuralgia by vasoconstrictor agents, *i.e.*, by the administration of benzedrine sulphate and subcutaneous epinephrine.[7]

It has been demonstrated that during the initial phases of anoxia, nerve cells and axones may have their thresholds lowered or may discharge spontaneously.[8] Furthermore, high intensity pain may result from pressure ischemia of the Gasserian ganglion and adjacent sensory root and nerves.[9] These data, demonstrating that cranial vasodilatation can eliminate pain and that impaired circulation and vasoconstriction about the head can precipitate pain, suggested that this apparent relation of the cranial circulation to tic douloureux should be further investigated.

MATERIAL AND METHODS

Only those patients were used for investigation who had "trigger areas" which, when experimentally stimulated, predictably produced pain. These patients, for varying periods of years, had had paroxysmal attacks of moderate or high intensity, burning and aching pain, lasting from one to sixty seconds, occurring singly or in series, spontaneously and after stimulation of "trigger areas" and precipitated by chewing, talking, laughing, swallowing, shaving or drinking cold water. The pain was limited to an area of the face innervated by one or more divisions of the fifth cranial nerve.

The seven patients so selected were instructed to indicate, on stimulation of the "trigger area," the moment of onset, the duration and the intensity of each attack. Before the action of any agent was studied a suitable "control" was established by experimentally inducing attacks of pain at three-minute intervals for twenty-one to thirty minutes. A vasodilator agent was then administered for varying periods, the patient meanwhile being stimulated at two- or three-minute intervals on the "trigger area," which during the control period had predictably elicited pain. When an agent was repeatedly administered during a period of two weeks, the "trigger area" was stimulated at stated intervals each day. The effects of such stimulation were recorded in terms of occurrence, duration and intensity of pain. The action of four vasodilator agents, known also to have an effect on intracranial vessels, histamine,[10] amyl nitrite,[11] ten per cent. carbon dioxide[12] and nicotinic acid[13,14] was investigated. In these experiments blood pressure changes never exceeded 20 mm of mercury above or below its initial level.

RESULTS

In all the patients both spontaneous and experimentally induced attacks of pain were diminished in intensity and duration, or eliminated by at least one of the vasodilator agents used. In most patients each of the four vasodilator agents was effective in modifying or eliminating attacks of pain during administration and for a short time thereafter. The additive effect of two agents, *i.e.*, nicotinic acid and amyl nitrite, could be demonstrated. Placebo procedures and agents did not have a similar effect. The vasodilator agents induced their effects usually some minutes after administration, either intravenous or by inhalation. Four minutes after nicotinic acid was given intravenously, attacks could no longer be induced for a thirty-minute period. There was occasionally a time interval of as long as sixty minutes between the beginning of administration and the onset of a major effect on tic. In several instances during the repeated administration of nicotinic acid (200 mg orally every four hours for two weeks) recurrence

[1] From the New York Hospital and the Departments of Medicine and Psychiatry, Cornell University Medical College, New York, N. Y.

[2] W. E. Dandy, *Am. Jour. Surg.*, 24: 447, 1934.

[3] F. H. Lewy and F. C. Grant, *Arch. Neur. and Psychiat.*, 40: 1126, 1938.

[4] P. G. Flothow, *Northwest Medicine*, 29: 69, 1930.

[5] R. E. McKechnie, *Canadian Med. Asn. Jour.*, 28: 41, 1933.

[6] M. J. Cooper, *Am. Jour. Med. Sci.*, 195: 83, 1938.

[7] W. E. Adams and W. Robinson, *Lancet*, 2: 555, 1941.

[8] Detlev W. Bronk, *Proc. Asn. Nerv. and Ment. Dis.*, 18: 298, 1937.

[9] Harvey Cushing, *Am. Jour. Med. Sci.*, 160: 157, 1920.

[10] H. S. Forbes, H. G. Wolff and S. Cobb, *Am. Jour. Physiol.*, 89: 266, 1929.

[11] H. G. Wolff, *Arch. Neurol. and Psychiat.*, 22: 686, 1929.

[12] H. G. Wolff and W. G. Lennox, *Arch. Neurol. and Psychiat.*, 23: 1097, 1930.

[13] C. D. Aring, H. D. Ryder, E. Roseman, M. Rosenbaum and E. B. Ferris, *Arch. Neurol. and Psychiat.*, 46: 649, 1941.

[14] M. T. Moore, *Arch. Int. Med.*, 65: 1, 1940.

of mild attacks of pain occurred when the patients were startled or when they were markedly anxious. In every patient sustained sensations of burning and aching were experienced over one or more divisions of the fifth nerve on the side of the tic for the first two to six days of nicotinic acid administration. Thereafter, in all but one patient, pain was eliminated during the short period of observation. It would appear that the paresthesias were due to partial ischemia because they were eliminated by inhaling amyl nitrite. In three patients nicotinic acid was effective in reducing the frequency and intensity of attacks for the first two days of administration, but then for two to three days spontaneous attacks occurred more frequently and were more intense, and attacks could be more readily induced experimentally. Thereafter, attacks of pain were eliminated. Cessation of administration of nicotinic acid was followed by a return of the attacks of pain, both the spontaneous and the experimentally induced. In some of these patients the recurrence of tic douloureux was first noted during episodes of anxiety or sudden physical activity.

In one patient an attack of tic douloureux was initiated at the peak of the pressor response when an extremity was immersed in ice water.

None of the vasodilator agents used raised the pain threshold.

CONCEPT OF MECHANISM

It is inferred from these observations that tic douloureux is the result of paroxysmal ischemia of trigeminal structures. The site of the ischemia may be central or peripheral. However, it is difficult to conceive of a central defect so circumscribed as to affect the function of only the trigeminal cells without involving adjacent nuclei and tracts. Also, such a defect must be so discrete as to produce pain limited to one or another division of the fifth cranial nerve. A peripheral ischemia involving Gasserian ganglion sensory root and nerves, however, could result in such a circumscribed disturbance. It is of interest that the vascular bed of the Gasserian ganglion is relatively poor.[15, 16] It is therefore postulated that afferent stimuli (touch, pressure, cold, muscle, etc.) arising from the "trigger area" evoke reflex vasoconstriction either widespread or local, but involving the trigeminal structures. Such reflex vasoconstriction alone, or more commonly when superimposed upon structurally narrowed vessels, results in a sudden and critical increase in ischemia and pain. This postulate is compatible with the observation that blocking such efferents by procaine or alcohol minimizes or eliminates tic douloureux for shorter or longer periods.

The short paroxysm of pain (from one to sixty seconds) can be understood as the effect of periodic vasoconstriction. In patients who are spontaneously having a series of attacks an episode of vasoconstriction may be followed by a short interval of improved blood supply, when the next of a series of vasoconstrictor episodes may induce another attack. Such phases may follow each other for one or more hours.

The time lapse between the administration of a vasodilator agent and reduction of the pain may be explained by assuming a cumulative effect of prolonged meager blood supply to nerve or a refractive state of the local blood vessels. The hyperalgesia of the skin over the painful area that occasionally occurs after a paroxysm of pain is compatible with a state of lowered pain threshold accompanying nerve ischemia.[8, 17]

In those patients who, when startled, apprehensive or subjected to immersion of an extremity in ice water, experience spontaneous attacks of pain, vasoconstriction within the trigeminal structures may be part of a widespread vasoconstrictor reflex or a response to a blood-borne pressor substance. In those patients in whom vasodilator agents modify the syndrome only slightly, structural changes in the blood vessels may be sufficiently advanced to prevent adequate vasodilatation. Because of individual variations in temperament, in the degree and rate of structural vascular changes and in tolerance to vasodilator agents, inferences about long term therapy are not justified. This study is focussed on the mechanism of pain in trigeminal neuralgia.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

SYNTHETIC LATEX AS INJECTION MASS FOR CLOSED VESSELS

THE use of natural latex as injection mass has been adequately discussed,[1, 2, 3, 4] but to our knowledge nothing has been published concerning synthetic latexes, although at present these are more available.

Two synthetic latex compounds have been used in the present work for vascular injection of cadavers. Present findings are based upon results of injection

[15] H. S. Dunning and H. G. Wolff, *Jour. Comp. Neur.*, 67: 433, 1937.

[16] H. G. Wolff, *Proc. Assn. Res. Nerv. and Ment. Dis.*, 18: 29, 1937 (see p. 52).

[17] N. Bigelow, I. Harrison, H. Goodell and H. G. Wolff, *Jour. Clin. Invest.*, in press, July, 1945.

[1] L. Petrovits and Z. Szabó, *Anat. Anz.*, Bd. 89, pp. 34–45, 1939.

of the entire arterial system in two cadavers, and regional injection, such as arms, legs and abdominal circulation, in an additional eleven cadavers.

The only advantage natural latex is found to possess is that of greater elasticity after it has set so that students may dissect with less danger of breaking or severing smaller twigs. However, synthetic latex mass becomes almost as tenuous, firm and flexible and is entirely satisfactory.

Synthetic latex was obtained from the manufacturer and color added before use. Cost of materials total approximately 75 cents per quart. Chemigum latex Type 100[5] to which has been added a finely divided insoluble water-borne red (A-2989 Toluidine toner)[6] behaves as natural latex and is used and handled with exactly the same technique.

Another latex used was Experimental Latex X-122[7] colored either with the water insoluble red as above or with a soluble dye (Chlorantine fast red 8-BLN).[8] This dye is used in concentrations not to exceed 0.4 per cent. of solids in a given amount of latex, and may be added directly to X-122. X-122 does not behave as natural latex, which coagulates suddenly on coming in contact with weak acid solutions, but may be injected into arteries without previously washing them out with weak ammonia solution.

Injections were made with a glass veterinary syringe, with rubber piston. An air pressure apparatus (5 to 7 pounds per square inch) did not provide sufficient force. Only one specimen had been recently embalmed. The others had been stored in vats for varying periods after embalming and took considerably less injection mass (40–50 per cent.) than can be put into soft pliable material.

Preparations of the cadavers were made through the femoral artery by injections in both directions—other limbs or organs were filled through the main artery normally supplying them. All sized arteries are readily filled. The arteries of the brain were well injected, also vasa vasorum and vasa nervorum as well as arterial anastomoses around joints.

The length of time required for coagulation is variable with the condition of the cadaver. Chemigum type 100 sets at about the same speed as natural latex. Latex X-122 requires a considerable period of time for setting so that preparations should be made several weeks before dissection is to be made. Each has advantages for special situations. X-122 would be preferable to use in a cadaver that had been stored in a vat for a long period. X-100 is more advantageous to use in an area which has been dissected or in mesenteric circulation, for if there is oozing through a rupture or a nick it can be coagulated by sponging with a weak acid solution and the hydraulic continuity of the vascular tubes restored, an impossibility if ligation is done. Also it is easier to sponge the surface of a vessel than to pick it up and tie it. Injection mass in exposed mesenteric circulation can be coagulated almost instantly by flooding the surface with weak acid and thus a preparation may be used immediately after injection.[9]

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[2] O. V. Batson, SCIENCE, 90: 518, 1939.
[3] D. P. Gamble, SCIENCE, 90: 520, 1939.
[4] E. E. Tobin, *Am. Jour. Roentgenology*, 51: 386–388, 1944.
[5] Goodyear, Akron 16, Ohio.
[6] Imperial Paper and Color Corporation, Glens Falls, N. Y.
[7] Dow Chemical Co., Midland, Mich.
[8] Ciba Company, New York, N. Y.

A NEW LABORATORY SHELLAC

THE recent scarcity of satisfactory shellac for the fixation and preservation of kymograph tracings made it imperative to look for satisfactory shellacking materials which can readily be made from ingredients commonly found in pharmacological and other biological laboratories.

At first from 10 to 20 per cent. alcoholic solutions of U.S.P. XII resin (colophony, white lump rosin obtained from the Arthur H. Thomas Company, Philadelphia) were used. These resins in such solutions, however, are quickly oxidized and the shellacked tracings become brittle. The best success was achieved by using the following formula: From 200 to 400 grams of rosin were dissolved in 2,000 cc of absolute or 95 per cent. alcohol; 400 cc of propylene glycol (resins are soluble in glycols) were added to the solution with 10–15 cc of castor oil as a plasticizing agent. The smoked tracing once immersed in this shellacking material must be allowed to dry for 12 hours, and then it may be rolled up and stored. The advantages of this new shellac is that records preserved with it do not become brittle, do not stick, and their surface does not become shiny. The tracings are easily photographed because of the lack of halation.

It may be added that ethylene glycol or other glycols may be used instead of propylene glycol to provide "body" and as antioxidants or any plasticizer may be used instead of castor oil. It is not to be assumed that the use of this shellac is limited to fixation of kymograph tracings.

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[9] Acknowledgments are due to all companies mentioned, for experimental material and suggestions. Dr. M. D. Overholser, head of the Department of Anatomy, has permitted generous use of departmental facilities and specimens.

DISCUSSION

INACTIVATION OF THE IRRITANT TOXICANTS OF POISON IVY AND POISON OAK

THE discovery of Sizer and Prokesch[1] that mushroom tyrosinase can render the poison of poison ivy (*Rhus Toxicodendron*) innocuous adds another oxidase to those already discovered which have this same property. However, all previous oxidases with the property of inactivating this (or these) poisons have been found in the poisonous *Rhus* sap along with the poison itself.[2]

It is of some interest to compare the clinical results of Sizer and Prokesch with those of Dr. Edward von Adelung. As the oxidase (or laccase) of western poison oak (*Rhus diversiloba*) has the power to change the poison to a non-toxic substance while exuded on the surface of an injured plant it was thought that this oxidase might change the poison to a non-toxic substance when on the human skin and thus be a remedy for Rhus dermatitis. Experiments were conducted by Edward von Adelung, M.D.[3] of Oakland, California, to ascertain the value of the enzyme solution as (1) poisonous or not; (2) a preventative of Rhus dermatitis; (3) remedy. The following results were obtained: (1) The enzyme solution did not produce dermatitis though rubbed briskly into the skin; (2) when mixed with Rhus poison in alcoholic solution it did not destroy the poison (the enzyme is active in 50 per cent. alcohol); (3) it had no remedial value.

However, it might be well to bear in mind that *Rhus diversiloba* oxidase is in all probability a different oxidase from the tyrosinase used by Sizer and Prokesch; and also that *Rhus diversiloba* poison may (or may not) be different from the poison of poison ivy (*Rhus Toxicodendron*).

It has been noticed by Bertrand that laccase (which apparently acts similarly to *Rhus diversiloba* oxidase) did not accelerate the oxidation of tyrosine but did accelerate the aerobic oxidation of guaiacol. On the other hand, he found mushroom tyrosinase to aid in the oxidation of tyrosine but not in that of guaiacol. Yet there is some similarity in the substracts acted upon by both enzymes; both enzymes oxidise some compounds containing mono- or polyhydroxy-phenyl groups. In the instance of tyrosinase this includes, as mentioned by Sizer and Prokesch, tyrosine and the sex hormones stilbestrol, estrone, a-estradiol or estriol. Therefore, one might have some expectation of finding the poisons of both poison oak and poison ivy to contain a mono- or polyhydroxy-phenyl group. That this is the case has been confirmed by the chemical analysis of several investigators. In regard to the poison of poison sumac (*Rhus Vernix*) being a hydroxylated compound, Stevens and Warren showed this to be the case as early as 1907. This was done by the use of the Grignard reagent. Stevens and Warren also observed that the magnesium organic halide, which resulted when the hydroxyl groups were destroyed by this reagent, was not toxic.

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[1] SCIENCE, 101: 517, 1945.

[2] H. Yoshida, *Jour. Chem. Soc.* (London) 43: 473–486, 1883; G. Bertrand, *Comptes rendus Acad. Sci.*, Paris, 18–145, 1894–1908 and *Bull. de la societe chimique de Paris*, 11– (3rd ser.) 4 (4th ser.), 1894–1908; A. B. Stevens, *Am. Jour. Pharm.*, 77: 255–260, 1905; A. B. Stevens and L. E. Warren, *Am. Jour. Pharm.*, 79: 499, 1907; J. B. McNair, *loc. cit.*

[3] J. B. McNair, *Jour. Infect. Dis.*, 20: 485–498, 1917; "Rhus Dermatitis," p. 69, 1923.

THE NAMES OF FOSSIL MEN

To the biologist working in other fields the significance implied by the names of fossil men is often misleading. He rather naturally concludes from such names as *Pithecanthropus erectus, Sinanthropus pekinensis* and *Eoanthropus dawsoni* that each is a distinct genus and species different from modern man. Furthermore, he believes that *Homo soloensis, H. rhodesiensis, H. heidelbergensis, H. neanderthalensis,* etc., connote types belonging to the same genus as does modern man but each to a different species.

However, to his dismay, he finds that his conclusions do not conform with those of some of the specialists on fossil man. Thus, Weidenreich,[1] one of the foremost contemporary authorities, states that all hominids, living and fossil, belong to the same species which is subdivided into several races or subspecies. This opinion is also held, on genetical grounds, by Dobzhansky.[2] In addition, Weidenreich[1] says that "The names given to groups and subgroups of fossil hominids have no 'generic' or 'specific' meaning. They are nothing but convenient labels, respected by tradition, to facilitate identification. I have used Sinanthropus and Pithecanthropus, etc., in this sense and shall continue to do so in the future." He also expels that famous "bone of contention," the Piltdown mandible, from the Hominidae and states that the name Eoanthropus should be discarded.

Most biologists believe that all living types of man belong to the same species, *Homo sapiens,* although Hill[3] and especially Gates[4, 5] have advanced evidence against this concept, the latter (Gates[5]) recognizing five species.

If all known men, living and fossil, do belong to the same species then the Linnear name, *Homo sa-*

[1] F. Weidenreich, "Palaeontologia Sinica." Whole Series 127: 1–484, 1943.

[2] T. Dobzhansky, *Am. Jour. Phys. Anthrop.*, n.s. 2: 251, 1944.

[3] W. C. Osman Hill, *Nature*, 145: 260, 1940.

[4] R. R. Gates, *Man*, 37: 28, 1937.

[5] *Idem. Am. Jour. Phys. Anthrop.*, n.s. 2: 279, 1944.

piens, would have priority over all the others and the various types of fossil men should be considered as subspecies of *H. sapiens.* In this case, the older scientific names, *e.g., Pithecanthropus erectus,* etc., would be inappropriate and should be abandoned. In their place could be substituted the names *Homo sapiens javanensis* (= *Pithecanthropus erectus*), *H. s. pekinensis* (= *Sinanthropus pekinensis*), *H. s. dawsoni* (= *Eoanthropus dawsoni,* if considered human), *H. s. rhodesiensis, H. s. heidelbergensis, H. s. neanderthalensis,* etc.

These names would be more in keeping with the usual rules of zoological nomenclature, would more clearly indicate the significance of the various types and would still readily distinguish the different fossil men, which is Weidenreich's sole reason for retaining the older names.

Another aid to other biologists would be a reduction in the synonymy. At present, to mention a few examples, *Homo neanderthalensis* = *Homo primigenius* or *Palaeoanthropus neanderthalensis; H. heidelbergensis* = *Palaeoanthropus heidelbergensis; H. soloensis* =*Palaeoanthropus soloensis, H. neanderthalensis soloensis* or *Javanthropus;* and *H. modjokertensis* = *Pithecanthropus erectus* (baby). In an earlier paper Weidenreich[6] calls *Pithecanthropus* by the name *Homo erectus javanensis* and *Sinanthropus* by the name *Homo erectus pekinensis,* but Dobzhansky[2] believes that the correct name for *Pithecanthropus* should be *Homo erectus erectus.*

Naturally, much of this confusion and synonymy can only be cleared up by further study and new material which would probably result in a change of status of some of the forms. However, whenever possible, the use of a single scientific name as the accepted and correct one is greatly to be desired.

The designation of the correct name, the status of the individual types and the reduction in the synonymy could probably be best and most efficiently brought about by an international board of experts. The fact that we are dealing with fossils, which are rarely complete specimens or abundant in number, greatly complicates the problem, as more than once in paleontology different generic and specific names have been given to various parts of the same individual or species. An additional factor contributing to the confusion is that human remains are among the rarest of fossils and it is undoubtedly extremely difficult for the discoverer or describer of a new specimen to be objective and unbiased in his evaluation of its true significance and importance.

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[6] F. Weidenreich, *Am. Anthropologist,* n.s. 42: 375, 1940.

THE REACTION OF VITAMIN A WITH LIEBERMAN-BURCHARD REAGENT

IN repeating the work of Lowman[1] on the reaction of vitamin A and carotene with adsorbed sulfuric acid it was found that unadsorbed sulfuric acid added to carotene in chloroform solution gave rise to a blue color. The difficulty that was encountered in attempted quantitative measurement of this color was the immiscibility of the sulfuric acid and the chloroform. However, when acetic anhydride was also added (Lieberman-Burchard reagent) the solution became completely homogeneous and gave rise to an intense blue-green color, which rapidly faded. Acetic anhydride by itself gave no color reaction when added to carotene.

This reaction was also obtained with vitamin A-carotene mixtures extracted from human blood plasma and suggests the possibility of utilizing this reaction for the quantitative measurement of vitamin A in plasma. One difficulty that might be encountered in such a determination would be the interference caused by cholesterol. This might be obviated by saponification of plasma cholesterol ester with mild alkali to free cholesterol and subsequent removal of cholesterol by precipitation with digitonin.

As time is not available for the complete study of the possibilities of this reaction this communication is being published as a suggestion to interested workers in the field.

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OPINION 152 OF THE INTERNATIONAL COMMISSION OF ZOOLOGICAL NOMENCLATURE[1]

ON May 24, 1944, the International Commission on Zoological Nomenclature issued Opinion 152 on the status of the generic names in the Order Diptera first published in 1800 by J. W. Meigen in his "Nouvelle Classification des Mouches à Deux Ailes."

This opinion has far greater importance than most workers realize, as it affects all branches of zoology. Few taxonomists know why the Meigen names have been the cause of so much discussion and therefore little realize the importance of this opinion.

In 1800, M. Baumhauer of Paris published a paper by J. W. Meigen entitled, "Nouvelle Classification des Mouches à Deux Ailes," in which he reviewed the known genera of Diptera and proposed many new genera. For all of these genera he gave names and short descriptions and cited the number of species, but gave no specific names. The generic descriptions

[1] A. Lowman, SCIENCE, 101: 183, February 16, 1945.

[1] Contribution No. 250 from the Entomology Department, University of Illinois, Urbana.

are very poor and have no diagnostic value as they are very incomplete. In the introduction, which has been overlooked by the majority of workers interested in this matter, appears the statement that this is a preliminary work, written for circulation among entomologists and would be followed by a more complete work. This indicated that Meigen did not wish these names to be used. In 1803 Meigen published a complete work on Diptera, but used none of the names he proposed in his 1800 paper. The 1800 paper was forgotten, but there is evidence that other workers of the time knew of it.

In 1908 F. Hendel[2] reprinted, in part, Meigen's paper of 1800. Hendel said he was able to recognize the 1800-genera by comparing the 1800 diagnoses (in French) with the diagnoses of the 1803 paper (in German) until he succeeded in pairing them off. He explicitly states that before he tried this method he was unable to recognize them from their diagnoses alone.

In 1909, J. M. Aldrich took steps to have the International Commission on Zoological Nomenclature act on the validity of the Meigen 1800 names. He sent them a paper, first asking if the 1800 names were valid and then listing reasons why they should not be, with the hope that the commission would declare that the names could not be or were not to be used. In 1910, the commission gave Opinion 28, which did not answer Aldrich's question, but stated that the 1800 paper had been published and, therefore, the names were available if found valid under the International Code. The majority of dipterists did not use the 1800 names, because they believed them invalid since they could not be recognized from the original description. Thus the matter rested until 1932, when F. W. Edwards of the British Museum published a "Questionnaire" in the *Entomologist* (65 (1932), pp. 13–14) and the *Entomologist Monthly Magazine* (vol. 68) (1932) pp. 1–3). The questions were as follows:

1. Do you consider that the names in the Nouvelle Classification should be accepted?
2. Do you consider that the omission of specific names renders the Nouvelle Classification names invalid?
3. Do you consider that, whether or not the Nouvelle Classification names are valid under the International Code, they should be annulled?

The results of the questionnaire were as follows (*Ent. Mo. Mag.*, vol. 68 (1932), pp. 255–258):

1. Affirmative, 13 per cent; no. of votes, 11.
2. Affirmative, 58 per cent; no. of votes, 58.
3. Affirmative, 74 per cent; no. of votes, 63.

The results show that the great majority of dipterists were definitely not in favor of the Meigen 1800 names.

[2] Verhandl. zool.-bot. Wien. Vol. 58 (1908), pp. 43–69.

In 1944, the commission issued Opinion 152, which stated, "The generic names in the Order Diptera (Class Insecta) first published in 1800 by J. W. Meigen in his 'Nouvelle Classification des Mouches à Deux Ailes' are to be treated as having priority as from that date." This opinion was issued in spite of the fact that the majority of dipterists were against using the Meigen 1800 names. Does this mean that the International Commission knows more about Diptera nomenclature than men who have spent their lifetime studying the subject? Secondly Opinion 152 shows that either the commission did not see a copy of the original 1800 paper or ignored Opinion 46, because it is impossible to recognize species from the generic descriptions as given in the 1800 paper.

The purpose of the International Commission on Zoological Nomenclature is to bring order to zoological nomenclature, but because of the ambiguous rules and opinions they have made, much of our nomenclature is no better than before the commission was formed. This matter of the Meigen 1800 names is an excellent example. So far they have given two opinions and neither has answered the question which was submitted for their consideration. They have simply said that it is up to the dipterist to interpret the meaning of their opinions. If it is up to the specialist to interpret the opinions why does the commission continue to publish ambiguous opinions? Are they afraid to offend some scientific worker by disagreeing with him?

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SCIENTIFIC PAPERS FOR EUROPE

SCIENTIFIC institutions in Europe are, as we all know, greatly in need of the technical literature which has appeared during the war, as well as older works to replace those lost owing to the war. Individual scientific workers can do a good service by sending their papers and others which they are able to obtain. I thought to make a beginning by sending a package of papers to the Congo Museum at Tervueren, Belgium, but it was returned to me as not complying with the necessary requirements. I was not told what these were, but in "News from Belgium," May 19, published by the Belgian Information Center in New York, I read:

The printed-matter service is restricted to:

(a) Periodicals and newspapers mailed directly by a publisher in this country to a publisher, an agent or a subscriber in Belgium.

(b) Other articles conforming to the conditions applicable to printed matter, mailed directly by a publisher or commercial firm.

Forwarding or remailing any article of printed matter for Belgium is prohibited. Publications containing technical data must comply with the licensing requirements of the Foreign Economic Administration.

These rules seem to be obstructionist and devoid of sense under present circumstances.

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SCIENTIFIC BOOKS

MANKIND

Mankind So Far. American Museum of Natural History Science Series. By WILLIAM HOWELLS. 319 pp. Illustrated. New York: Doubleday, Doran and Company, Inc. 1944. $4.50.

THE book comprises three parts of about 100 pages each: Animals and the Coming of Man, Man and the Coming of Homo Sapiens and, finally, Homo Sapiens and the Coming of Races. In the words of the author, "Of all animals we men are the only ones who wonder where we came from and where we will go." Science has given much serious attention to the successive appearances of man-like creatures, patiently collecting the evidence upon which a reconstruction of his lost history could be based to the end that much new data have been accumulated during the half century now closing. Hence there is need for a clear logical attempt at such reconstruction. Until the appearance of this volume, there was no high-class treatise which the anthropologist could recommend to the scholar as well as to the intelligent lay reader seeking a reliable summary of the subject.

As may be expected, the first part of the book deals with the predecessor of man and could be consistently labeled "from fish to man," a favorite headline in current museum exhibits. The common saying that "scientists agree on nothing" is not strictly true, since paleontologists and anthropologists usually agree that no creatures properly designated as *Hominidae* are known before the Pleistocene Epoch, the régime of the Ice Ages, when, in the words of the author, "the weather was certainly something to talk about." In this section of the book, the author follows closely the broad generalizations of paleontology, but not blindly, since now and then he questions traditional interpretations. In his remarks about fire and cooking, he reveals an honest doubt that fire was so necessary for warmth as to force its invention and use since caves are usually warm enough, but that cooking and a liking for novelty may claim priority as a motive. In more general terms, the author suspects that "fire, flintworking, speech and society" served to increase man's numbers rather than to change his anatomy. However, he looks favorably upon the idea that the increase in numbers due to revolutionary inventions, such as fire, the bow, domestication, etc., might increase individual and group variation, thus leading to the wide range of race diversity in modern mankind. He rejects as unscientific the idea that man somehow sensed a career upon the ground as more desirable than one in the trees. Nevertheless, he imagines there was a great hazard in such a shift because the evolution of a foot was necessary, as the lack of it dooms the chimpanzee and the gorilla to extinction.

The over-all puzzle in the story of the several known species of the genus *Homo* is to reconcile the disappearance of all these species save one, *sapiens,* with the wide variations conceived as entities which we speak of as races. Yet the author reminds us that we are prone to grossly exaggerate these differences, to the end that we really think of "our races" as species, many of us unconsciously running amuck by giving them genus rank. He shows us that anthropologists favor one or the other of two opposing theses: (a) that none of the species of *Homo* save one, *sapiens,* was able to survive the selective rigor of the Pleistocene, but that even his grasp upon the continuity of morphological form was so shattered that he survived in a number of variations of near-species grade; (b) that few, if any, of these early species really disappeared, but that after an interval began a rapid transition by convergent evolution (by no means ended) accelerated by what we call "race mixture," so far leaving us a few sharply marked varieties of man no longer worthy of being rated as separate species. Of contemporary anthropologists, Weidenreich leads in support of *b,* whereas the author of this book bids for leadership in the *a* group. He contends that among the many objections to accepting theory *b* are that it violates the principles of genetics and is out-of-step with comparative morphology, but holds that neither view should be taken too seriously, because the number of available fossils of man is contemptibly small in contrast to the millions of examples of *Homo sapiens.* If new finds of fossil man are made, a less puzzling answer may be forthcoming.

We come now to the third section of the book. Since it is the custom to speak of the varieties of *Homo sapiens* as races, the author accepts that term with the title "Homo Sapiens and the Coming of Races." Beginning with the three great primary strains, White, Yellow and Black, there follow another

hundred pages of interesting condensed discussion, the most satisfactory brief characterization we have seen. Other writers have found this task baffling, leading the reader into hopeless confusion. Possibly one secret in the author's art is that he combines time perspective with plain geographical distribution, thus giving sketches of modern man which can be sensed in terms of the cardinal points—and a fifth dimension, called time. It follows that no one could achieve such a literary triumph without a profound knowledge of the facts of distribution in all these dimensions, in research and years of experience in skilful teaching. Further, limitations of space may have led the author to change his method; whereas in the other two sections of the book he has clearly stated the divergent theories of the leading writers, in this he ignores such contributions as are not easily classified or reduced to simple statements, giving instead his own views of race origins and migrations. A good example of this is the treatment of the Negro and Negroid problems. Whereas in the case of the American Indian, he accepts and follows the traditional American interpretation of an Asiatic origin, he treats the Negro by some bold generalizations, without hinting that many more definite yet often ill-grounded theories are entertained by recognized anthropologists, but begins with a unique diagrammatic ethnographic map of Africa which, for clearness, leaves little to be desired. He then turns to the African Whites, whose restricted habitat seems to be North Africa, an ancient physiographic part of Europe. He sees these White people streaming into Africa by way of the Suez "bottle-neck," but ignores the question as to how the Negro came to be in the Central African forests to assist in forming the intervening Sudan by mixing with the White intruders from the north. The Bushmen of South Africa are accepted as the traditional early inhabitants, while the Pygmies are passed over as a hopeless puzzle as are certain of the Negroids and Negritoes in eastern Asia, startling the reader with the suggestion that both Pygmies and Negroes may be foreigners in Africa.

Nevertheless, a perusal of these hundred pages leaves one with a clear lively picture of where the many varieties of the world's peoples were settled when European navigators "unrolled the map of the world about 1500," and formulates the most pertinent questions that can be asked concerning them even though satisfactory answers are not forthcoming. Whatever weaknesses the book may have are justifiable omissions rather than mis-statements of fact. The appearance of so readable and reliable a book dealing with the races of man is an important scientific achievement.

CLARK WISSLER

GENERAL CHEMISTRY

Introductory General Chemistry. Third edition. By STUART R. BRINKLEY. x + 645 pp. 135 figs. New York: The Macmillan Company, 1945. $4.00.

THIS book is shorter by 32,000 words, or the equivalent space (86 pages) than the preceding revised edition of 1938. It has been extensively rewritten with some changes in the order of presentation and considerable modernization of the factual and theoretical content. The general style is the same: basic considerations, fundamental laws and theory are compressed into the first 30 pages, plus 10 pages later on molecular and atomic weights; the description of chemical substances, reactions and processes is adequate and modern, though brief; the book is built around the presentation of principles and theory with a definite effort to keep illustrative material adequate but at a minimum. Although entitled "Introductory" its use should presuppose a good course in secondary school chemistry or a selected group of students.

A great deal of space is devoted to applications of the modern theories of aqueous solutions. This includes emphasis on the ionic nature of reactions, the ion-electron treatment of oxidation-reduction reactions with many detailed illustrations, and extensive application of the Brönsted point of view to acidic and basic molecules and ions. The revision with respect to the acid-base theory is an outstanding feature of this edition. The difference between the dispersal of salt ions in water and the formation of ions from molecular acids is made clear. Anion and cation acids, molecular and ionic bases are discussed. The hydrolysis of salts is presented in terms of the acidic and basic properties of their ions. Throughout the chapters on the metals the hydration of metal ions and hydroxides is emphasized. This unfortunately leads to cumbersome formulas and equations, and sometimes alternate equations are given, omitting water of hydration.

This will not be an easy book to study; it is a serious, technical book, and for the serious chemistry major it will give an excellent background for subsequent courses.

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BOOKS RECEIVED

BINGHAM, MARJORIE T. *Flora of Oakland County, Michigan.* Illustrated. Pp. 155. Cranbrook Institute of Science. $1.00. 1945.

CANNON, WALTER B. *The Way of an Investigator; A Scientist's Experiences in Medical Research.* Pp. 229. W. W. Norton & Company. $3.00. 1945.

DUBOS, RENÉ J. *The Bacterial Cell.* Illustrated. Pp. xix + 460. Harvard University Press. $5.00.

GRINKER, ROY R. and JOHN P. SPIEGEL. *Men under Stress.* Pp. xii + 484. The Blakiston Company. 1945.

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